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| NEWS 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS 2 | Apr 08 | "Ask CAS" for self-help around the clock |
| NEWS 3 | Apr 09 | BEILSTEIN: Reload and Implementation of a New Subject Area |
| NEWS 4 | Apr 09 | ZDB will be removed from STN |
| NEWS 5 | Apr 19 | US Patent Applications available in IFICDB, IFIPAT, and IFIUDB |
| NEWS 6 | Apr 22 | Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS |
| NEWS 7 | Apr 22 | BIOSIS Gene Names now available in TOXCENTER |
| NEWS 8 | Apr 22 | Federal Research in Progress (FEDRIP) now available |
| NEWS 9 | Jun 03 | New e-mail delivery for search results now available |
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| NEWS 11 | Jun 10 | PCTFULL has been reloaded |
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| NEWS 13 | Jul 22 | USAN to be reloaded July 28, 2002; saved answer sets no longer valid |
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| NEWS 17 | Aug 08 | PHARMAMarketLetter(PHARMAML) - new on STN |
| NEWS 18 | Aug 08 | NTIS has been reloaded and enhanced |
| NEWS 19 | Aug 19 | Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN |
| NEWS 20 | Aug 19 | IFIPAT, IFICDB, and IFIUDB have been reloaded |
| NEWS 21 | Aug 19 | The MEDLINE file segment of TOXCENTER has been reloaded |
| NEWS 22 | Aug 26 | Sequence searching in REGISTRY enhanced |
| NEWS 23 | Sep 03 | JAPIO has been reloaded and enhanced |
| NEWS 24 | Sep 16 | Experimental properties added to the REGISTRY file |
| NEWS 25 | Sep 16 | CA Section Thesaurus available in CAPLUS and CA |
| NEWS 26 | Oct 01 | CASREACT Enriched with Reactions from 1907 to 1985 |
| NEWS 27 | Oct 21 | EVENTLINE has been reloaded |
| NEWS 28 | Oct 24 | BEILSTEIN adds new search fields |
| NEWS 29 | Oct 24 | Nutraceuticals International (NUTRACEUT) now available on STN |
| NEWS 30 | Oct 25 | MEDLINE SDI run of October 8, 2002 |
| NEWS 31 | Nov 18 | DKILIT has been renamed APOLLIT |
| NEWS 32 | Nov 25 | More calculated properties added to REGISTRY |
| NEWS 33 | Dec 02 | TIBKAT will be removed from STN |
| NEWS 34 | Dec 04 | CSA files on STN |
| NEWS 35 | Dec 17 | PCTFULL now covers WP/PCT Applications from 1978 to date |
| NEWS 36 | Dec 17 | TOXCENTER enhanced with additional content |
| NEWS 37 | Dec 17 | Adis Clinical Trials Insight now available on STN |
| NEWS 38 | Dec 30 | ISMEC no longer available |
| NEWS 39 | Jan 21 | NUTRACEUT offering one free connect hour in February 2003 |
| NEWS 40 | Jan 21 | PHARMAML offering one free connect hour in February 2003 |
| NEWS 41 | Jan 29 | Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC |
| NEWS 42 | Feb 13 | CANCERLIT is no longer being updated |
| NEWS 43 | Feb 24 | METADEX enhancements |

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NEWS 44   Feb 24  PCTGEN now available on STN
NEWS 45   Feb 24  TEMA now available on STN
NEWS 46   Feb 26  NTIS now allows simultaneous left and right truncation
NEWS 47   Feb 26  PCTFULL now contains images
NEWS 48   Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 49   Mar 19  APOLLIT offering free connect time in April 2003
NEWS 50   Mar 20  EVENTLINE will be removed from STN
NEWS 51   Mar 24  PATDPAFULL now available on STN
NEWS 52   Mar 24  Additional information for trade-named substances without
                  structures available in REGISTRY
NEWS 53   Mar 24  Indexing from 1957 to 1966 added to records in CA/CAPLUS

NEWS EXPRESS  January 6 CURRENT WINDOWS VERSION IS V6.01a,
              CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS    STN Operating Hours Plus Help Desk Availability
NEWS INTER    General Internet Information
NEWS LOGIN    Welcome Banner and News Items
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=> FIL MEDLINE BIOSIS EMBASE CA SCISEARCH
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

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=> s (interleukin (n) 8) or (IL (2n) 8) or (beta (n) thromboglobulin (n) like (n)
protein) or mdncf or monap
L1        56227 (INTERLEUKIN (N) 8) OR (IL (2N) 8) OR (BETA (N) THROMBOGLOBULIN
                (N) LIKE (N) PROTEIN) OR MDNCF OR MONAP
```

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=> s (monocyte (n) derived neutorphoil chemotactic factor) or (monocyte (n) derived
neutorphil activating protein)
L2            0 (MONOCYTE (N) DERIVED NEUTORPHOIL CHEMOTACTIC FACTOR) OR (MONOCY
                TE (N) DERIVED NEUTORPHIL ACTIVATING PROTEIN)

=> s (monocyte (n) derived neutrophil chemotactic factor) or (monocyte (n) derived
neutrophil activating protein)
L3          126 (MONOCYTE (N) DERIVED NEUTROPHIL CHEMOTACTIC FACTOR) OR (MONOCYT
                E (N) DERIVED NEUTROPHIL ACTIVATING PROTEIN)

=> s lect or luct or scyb8
L4          571 LECT OR LUCT OR SCYB8

=> s l1 or l2 or l3 ro l4
MISSING OPERATOR L3 RO
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l1 or l2 or l3 or l4
L5        56776 L1 OR L2 OR L3 OR L4

=> s antisense or (compleme? (2n) (oligonucl? or nucl?))
L6       118587 ANTISENSE OR (COMPLEME? (2N) (OLIGONUCL? OR NUCL?))

=> s l5 and l6
L7          440 L5 AND L6

=> s l7 and (inhib? or regu? or modif?)
L8          362 L7 AND (INHIB? OR REGU? OR MODIF?)

=> s l7 and ((inhib? or regu? or modif?) (s) l6)
   3 FILES SEARCHED...
L9          270 L7 AND ((INHIB? OR REGU? OR MODIF?) (S) L6)

=> s l7 and ((inhib? or regu? or modif?) (5n) l6)
   3 FILES SEARCHED...
L10         115 L7 AND ((INHIB? OR REGU? OR MODIF?) (5N) L6)

=> dup rem
ENTER L# LIST OR (END):l10
PROCESSING COMPLETED FOR L10
L11          56 DUP REM L10 (59 DUPLICATES REMOVED)

=> s l11 py<=2001
MISSING OPERATOR L11 PY<=2001
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l11 and py<=2001
   2 FILES SEARCHED...
L12          48 L11 AND PY<=2001

=> d l12 1-48 ibib abs

L12  ANSWER 1 OF 48     MEDLINE
ACCESSION NUMBER:   2001634969     MEDLINE
DOCUMENT NUMBER:    21230885   PubMed ID: 11332197
TITLE:              Protection of mice from LPS-induced shock by CD14
                    antisense oligonucleotide.
AUTHOR:             Furusako S; Takahashi T; Mori S; Takahashi Y; Tsuda T;
                    Namba M; Mochizuki H
```

CORPORATE SOURCE: Research Center, Mochida Pharmaceutical Co., Ltd., Shizuoka 412-8524, Japan.
SOURCE: ACTA MEDICA OKAYAMA, **(2001 Apr)** 55 (2) 105-15.
Journal code: 0417611. ISSN: 0386-300X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200111
ENTRY DATE: Entered STN: 20011105
Last Updated on STN: 20011105
Entered Medline: 20011101

AB CD14 is a pattern recognition receptor on myeloid cells and plays a pivotal role in an innate immune system that is responsible for Gram-negative and Gram-positive bacteria infection. Lipopolysaccharide (LPS), a cell wall component of Gram-negative bacteria, can induce production of a large quantity of proinflammatory cytokines into the circulation mediated by CD14-mediated macrophages and monocytes. These cytokines eventually cause septic shock. Several in vitro and in vivo studies have shown that suppression of a CD14 function by a CD14 antibody led to an inhibition of the production of proinflammatory cytokines such as TNF-alpha, IL-1 beta, and **IL-8**. In the present study, we found that CD14 **antisense** oligonucleotide (ODN) can prevent lethal LPS shock in D-galactosamine-sensitized mice. This ODN inhibited CD14 expression in a mouse macrophage cell line, RAW264.7, and suppressed production of TNF-alpha in LPS-stimulated RAW264.7 cells. Furthermore, we designed a consensus **antisense** ODN that could hybridize human and mouse CD14 RNA, and we evaluated its efficacy. The consensus **antisense** ODN rescued mice primed with Mycobacterium bovis bacillus Calmette-Guerin (BCG) from the LPS-induced lethal shock. In this model, the CD14 **antisense** ODN down-**regulated** LPS-elicited CD14 expression in the liver, resulting in a decrease in LPS-induced TNF-alpha production. These findings suggest that the CD14 **antisense** ODN is distributed in the liver and efficiently suppresses LPS-induced TNF-alpha production by reducing CD14 expression on Kupffer cells. This CD14 **antisense** ODN may be useful for the development of a therapeutic agent against sepsis and septic shock.

L12 ANSWER 2 OF 48 MEDLINE
ACCESSION NUMBER: 2001413366 MEDLINE
DOCUMENT NUMBER: 21336622 PubMed ID: 11349132
TITLE: P2Y(6) nucleotide receptor mediates monocyte **interleukin-8** production in response to UDP or lipopolysaccharide.
AUTHOR: Warny M; Aboudola S; Robson S C; Sevigny J; Communi D; Soltoff S P; Kelly C P
CORPORATE SOURCE: Gastroenterology Divison, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts 02215, USA.. mwarny@caregroup.harvard.edu
CONTRACT NUMBER: RO1DK54290 (NIDDK)
RO1DK58858 (NIDDK)
RO1HL57307 (NHLBI)
RO1HL63972 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(2001 Jul 13)** 276 (28) 26051-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820

Last Updated on STN: 20030105
Entered Medline: 20010816

AB Extracellular nucleotides are autocrine and paracrine cellular mediators that signal through P2 nucleotide receptors. Monocytic cells express several P2Y receptors but the role of these G protein-coupled receptors in monocytes is not known. Here, we present evidence that P2Y(6) regulates chemokine production and release in monocytes. We find that UDP, a selective P2Y(6) agonist, stimulates interleukin (**IL**)-**8** release in human THP-1 monocytic cells whereas other nucleotides are relatively inactive. P2 receptor antagonists or P2Y(6) **antisense** oligonucleotides **inhibit** **IL-8** release induced by UDP. Furthermore, UDP specifically activated **IL-8** production in astrocytoma 1321N1 cells transfected with human P2Y(6). Since lipopolysaccharide has been suggested to activate P2 receptors via nucleotide release, we tested whether **IL-8** production stimulated by lipopolysaccharide might result from P2Y(6) activation. P2 antagonists or apyrase, an enzyme which hydrolyzes nucleotides including UDP, inhibit **IL-8** production induced by lipopolysaccharide but not by other stimuli. Furthermore, **IL-8** gene expression activated by lipopolysaccharide is enhanced by P2Y(6) overexpression and **inhibited** by P2Y(6) **antisense** oligonucleotides. Thus, UDP activates **IL-8** production via P2Y(6) in monocytic cells. Furthermore, lipopolysaccharide mediates **IL-8** production at least in part by autocrine P2Y(6) activation. These findings indicate a novel role for P2Y(6) in innate immune defenses.

L12 ANSWER 3 OF 48 MEDLINE
ACCESSION NUMBER: 2001017868 MEDLINE
DOCUMENT NUMBER: 20361490 PubMed ID: 10905555
TITLE: **Antisense** oligomers for selective suppression of MCP-1 synthesis in human pulmonary endothelial cells.
AUTHOR: Maus U A; Herold S; Schlingensiepen K H; Schlingensiepen R; Dormayr T; Rosseau S; Maus R; Seeger W; Lohmeyer J
CORPORATE SOURCE: Department of Internal Medicine, Justus-Liebig-University, Giessen, Germany.
SOURCE: ANTISENSE AND NUCLEIC ACID DRUG DEVELOPMENT, **(2000 Jun)** 10 (3) 185-93.
Journal code: 9606142. ISSN: 1087-2906.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001109

AB Endothelial synthesis of the C-C chemokine monocyte chemotactic protein-1 (MCP-1) has been implicated in the regulation of monocyte recruitment for extravascular pools under both physiologic and inflammatory conditions. We designed and characterized five **antisense** phosphorothioate oligodeoxynucleotides (PS-ODN) targeting MCP-1 secretion by human pulmonary artery endothelial cells (HPAEC) and pulmonary microvascular endothelial cells (HMVEC-L). The most effective PS-ODN (MCP-1 AS 2) dose-dependently suppressed the secretion of MCP-1 but not the secretion of the C-X-C chemokine **interleukin-8** (**IL-8**) in both HPAEC and HMVEC-L in the nanomolar concentration range. Mismatch controls bearing 2 or 4 bp substitutions showed markedly reduced inhibitory capacity. MCP-1 mRNA levels were not affected even at the highest PS-ODN doses employed (ribonuclease protection assay), suggesting a translational arrest of MCP-1 production. Accordingly, PS-ODN exhibited no nonspecific side effects on immediate-early gene regulation of the

transcription factor nuclear factor-kappaB (NF-kappaB), as analyzed by gel shift assays. **Antisense** pretreatment of HPAEC reduced the monocyte chemotactic bioactivity liberated from tumor necrosis factor-alpha (TNF-alpha)-activated endothelial cells (EC) and reduced the TNF-alpha-induced transendothelial monocyte migration. We conclude that nanomolar concentrations of specific **antisense** oligodeoxynucleotides effectively **inhibit** human endothelial MCP-1 synthesis and may thus provide a rational approach to modulate monocyte recruitment under inflammatory conditions.

L12 ANSWER 4 OF 48 MEDLINE
ACCESSION NUMBER: 2000125662 MEDLINE
DOCUMENT NUMBER: 20125662 PubMed ID: 10657945
TITLE: Thrombin upregulates **interleukin-8** in lung fibroblasts via cleavage of proteolytically activated receptor-I and protein kinase C-gamma activation.
AUTHOR: Ludwicka-Bradley A; Tourkina E; Suzuki S; Tyson E; Bonner M; Fenton J W 2nd; Hoffman S; Silver R M
CORPORATE SOURCE: Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, South Carolina 29425, USA.
CONTRACT NUMBER: RR1070-1 (NCRR)
SOURCE: AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY, **(2000 Feb)** 22 (2) 235-43.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000309

AB Acute and chronic interstitial lung diseases are accompanied by evidence of inflammation and vascular injury. Thrombin activity in bronchoalveolar lavage fluid from such conditions is often increased, as well as interleukin (**IL**)-**8**. We observed that conditioned medium from lung fibroblasts exposed to thrombin has chemotactic activity for polymorphonuclear cells, and that this activity can be abolished by antibody to **IL-8**. We report that thrombin stimulates expression of **IL-8** in human lung fibroblasts on both the messenger RNA and protein levels in a time- and dose-dependent manner. Stimulation of **IL-8** expression by thrombin is inhibited by specific thrombin inhibitors. Synthetic thrombin receptor agonist peptide-14 mimics thrombin's stimulation of **IL-8** expression in a dose-dependent manner consistent with the idea that upregulation of **IL-8** by thrombin in human lung fibroblasts requires cleavage of proteolytically activated receptor-I. We demonstrate further that thrombin-induced **IL-8** synthesis is regulated by protein kinase (PK) C. PKC-gamma may be involved in the upregulation of lung fibroblast **IL-8** by thrombin because stimulation of lung fibroblasts with thrombin caused significant upregulation of PKC-gamma and because PKC-gamma **antisense** oligonucleotides **inhibited** the accumulation of PKC-gamma protein and **IL-8** protein. Our data suggest that the PKC-gamma isoform increase observed after thrombin stimulation is required for thrombin-induced **IL-8** formation by human lung fibroblasts.

L12 ANSWER 5 OF 48 MEDLINE
ACCESSION NUMBER: 2000120754 MEDLINE
DOCUMENT NUMBER: 20120754 PubMed ID: 10653823

TITLE: Laminar shear stress upregulates the complement-inhibitory protein clusterin : a novel potent defense mechanism against complement-induced endothelial cell activation.
AUTHOR: Urbich C; Fritzenwanger M; Zeiher A M; Dimmeler S
CORPORATE SOURCE: Molecular Cardiology, Department of Internal Medicine IV, University of Frankfurt, Germany.
SOURCE: CIRCULATION, **(2000 Feb 1)** 101 (4) 352-5.
Journal code: 0147763. ISSN: 1524-4539.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Space Life Sciences
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000309
Last Updated on STN: 20010521
Entered Medline: 20000218

AB BACKGROUND: The complement system is implicated in the pathogenesis of atherosclerosis. Complement has been shown to activate endothelial cells (ECs) by inducing a proinflammatory response. Physiological levels of shear stress exert potent antiatherosclerotic effects. Therefore, we investigated whether shear stress antagonizes the effects of complement on ECs. METHODS AND RESULTS: Incubation of ECs with nonlytic concentrations of complement serum (CS: 0.2 U/mL for 6 hours) resulted in an upregulation of **interleukin-8** (**IL-8**) (165+/-12%) and monocyte chemoattractant protein-1 (MCP-1) mRNA expression (267+/-34%). Preexposure of ECs for 18 hours with laminar shear stress (15 dyne/cm(2)) abrogated CS-induced **IL-8** release to 106+/-10% ($P<0.001$) and reduced CS-induced MCP-1 expression (170+/-31%; $P<0.05$). To examine the mechanism of the protective effect of shear stress, expression of the complement-inhibitory protein clusterin was analyzed under shear exposure. Shear stress increased clusterin mRNA (225+/-76%, 6 hours) and protein expression (164+/-22%, 18 hours). Specific **inhibition** of clusterin by transfection with **antisense** oligonucleotides reversed the protective effect of shear stress on CS-induced MCP-1 and **IL-8** upregulation ($P<0.05$ versus sense-transfected cells). Moreover, clusterin overexpression inhibited CS-induced EC activation. CONCLUSIONS: Shear stress abrogates the complement-induced proinflammatory response of ECs by upregulation of the complement-inhibitory protein clusterin. Upregulation of clusterin may contribute to the potent antiatherosclerotic effects of shear stress by preventing endothelial activation through the complement cascade.

L12 ANSWER 6 OF 48 MEDLINE
ACCESSION NUMBER: 2000029297 MEDLINE
DOCUMENT NUMBER: 20029297 PubMed ID: 10565567
TITLE: **Antisense** IRAK-2 oligonucleotide blocks IL-1-stimulated NF-kappaB activation and ICAM-1 expression in cultured endothelial cells.
AUTHOR: Guo F; Li Y; Wu S
CORPORATE SOURCE: Institute of Pharmaceutic Sciences, The First Military Medical University, Guang Zhou, China.
SOURCE: INFLAMMATION, **(1999 Dec)** 23 (6) 535-43.
Journal code: 7600105. ISSN: 0360-3997.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113

Entered Medline: 19991130

AB Phosphorothioate oligodeoxynucleotide (ODN) was designed **antisense** to sequences of the recently cloned human IL-1 receptor associated kinase-2 (IRAK-2). **Antisense** IRAK-2 ODN was delivered by lipofectin encapsulation into cultured endothelial cells. The levels of NF-KB, surface expression of intracellular adhesion molecule-1 (ICAM-1), ICAM-1 and IRAK-2 mRNAs were measured by sandwich ELISA, ELISA on cells in situ, and semiquantitative reverse transcription-PCR (RT-PCR), respectively. **Antisense** IRAK-2 ODN **inhibited** IL-1-induced NF-KB activation and surface expression of ICAM-1 in a concentration (1-4 microg)- and time (5-24 h)-dependent fashion. A maximum inhibition of NF-KB activation or surface expression of ICAM-1 occurred when the cells were incubated with **antisense** IRAK-2 ODN 3 microg for **8** h. **IL**-1-induced ICAM-1 mRNA expression was also **inhibited** after treatment of cells with **antisense** IRAK-2 ODN 3 microg for 8 h. The attenuation of the cellular response to IL-1 caused by **antisense** IRAK-2 ODN correlated with a reduction of IRAK-2 expression. These data suggest that **antisense** IRAK-2 ODN may share a role in the design of antiinflammatory therapeutics.

L12 ANSWER 7 OF 48 MEDLINE
ACCESSION NUMBER: 1999388447 MEDLINE
DOCUMENT NUMBER: 99388447 PubMed ID: 10454982
TITLE: Achieving **antisense inhibition** by oligodeoxynucleotides containing N(7)-modified 2'-deoxyguanosine using tumor necrosis factor receptor type 1.
AUTHOR: Ojwang J O; Rando R F
CORPORATE SOURCE: ZymeTx, Inc., 800 Research Parkway, Suite 100, Oklahoma City, Oklahoma, 73104-3600,. USA.. ojwang@zymetx.com
SOURCE: METHODS, **(1999 Jul)** 18 (3) 244-51.
Journal code: 9426302. ISSN: 1046-2023.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990916

AB **Antisense** oligodeoxynucleotides (ODNs) are being explored as therapeutic agents for the treatment of many disorders including viral infections, cancers, and inflammatory disorders. In addition, **antisense** technology can be of great benefit to those attempting to assign function to the multitude of new genes being uncovered in the genomics initiative. However, the demonstration that the gene-**regulating** effects produced by **antisense**-designed ODNs are attributable to an **antisense** mechanism of action requires carefully designed experimentation. Critical to the assignment of an **antisense** mechanism of action is the availability of nuclease-stable ODNs, inside cells, that have a high binding affinity with the target mRNA and modulate gene functions in a sequence-dependent manner. To help us achieve a goal of sequence-specific **antisense** activity we designed **antisense** ODNs containing C(5)-propyne-**modified** 2'-deoxyuracil and N(7)-propyne-modified 7-deaza-2'-deoxyguanosine bases and partially modified (phosphorothioate) internucleoside linkages. These modified ODNs were found to have enhanced binding affinity to their target mRNA sequences as well as reduced sequence-independent side effects. We used these ODNs to specifically inhibit p55 tumor necrosis factor receptor type 1 expression and tumor necrosis factor alpha-mediated functions in culture assays.

Adenis

L12 ANSWER 8 OF 48 MEDLINE
ACCESSION NUMBER: 1998427309 MEDLINE
DOCUMENT NUMBER: 98427309 PubMed ID: 9755878
TITLE: Effect of **interleukin-8** on production of tumor-associated substances and autocrine growth of human liver and pancreatic cancer cells.
AUTHOR: Miyamoto M; Shimizu Y; Okada K; Kashii Y; Higuchi K; Watanabe A
CORPORATE SOURCE: The Third Department of Internal Medicine, Faculty of Medicine, Toyama Medical and Pharmaceutical University, Toyama City, Japan.
SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, **(1998 Sep)** 47 (1) 47-57.
Journal code: 8605732. ISSN: 0340-7004.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981016

AB We have previously reported that human liver cancer cell lines produce **interleukin-8** (**IL-8**) at high levels. Those tumor cells appeared to express two kinds of **IL-8** receptor on their surface. In order to analyze the role of **IL-8** on the biological characteristics of those tumor cells, we suppressed **IL-8** production from human liver (HuH-7 and HuCC-T1) and pancreatic cancer cell lines (HuP-T4) by treatment with **IL-8 antisense** oligonucleotides. Suppression of **IL-8** production resulted not only in inhibition of cell growth, but also in an increase in the concentrations of some tumor-associated substances such as carbohydrate antigen 19-9 (CA19-9) in the medium. These data indicate that **IL-8** produced by human liver and pancreatic tumors may act as an autocrine growth factor and may control the production of some tumor-associated substances. Furthermore, surface expression of sialyl-Lewis(a), which is a ligand for ELAM-1 on human umbilical vein endothelial cells (HUVEC), HuCC-T1 and HuP-T4 cells was decreased and the attachment of these tumor cells to HUVEC was **inhibited** by treatment with **IL-8 antisense** oligonucleotide. Since the soluble form of CA19-9 (sialyl-Lewis(a)) was shown to inhibit the tumor cell binding to HUVEC, the decrease in release of CA19-9 into the medium and increase in the expression of sialyl-Lewis(a) on the cell surface may suggest that **IL-8** production from the tumor cells enhances metastatic potential by augmenting the binding activity of the tumor cells to HUVEC. These data demonstrate that a cytokine produced by tumor cells may function as an autocrine growth factor and affect tumor cell dissemination.

L12 ANSWER 9 OF 48 MEDLINE
ACCESSION NUMBER: 1998202141 MEDLINE
DOCUMENT NUMBER: 98202141 PubMed ID: 9543141
TITLE: **Interleukin-8** induces proliferation of endometrial stromal cells: a potential autocrine growth factor.
AUTHOR: Arici A; Seli E; Zeyneloglu H B; Senturk L M; Oral E; Olive D L
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, Connecticut 06520, USA.. Aydin.Arici@Yale.edu

Adenis

CONTRACT NUMBER: HD-01041 (NICHD)
SOURCE: JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, **(1998 Apr)** 83 (4) 1201-5.
~~Journal code: 0375362. ISSN: 0021-972X.~~
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980430
Last Updated on STN: 19980430
Entered Medline: 19980421

AB Proliferation of endometrium is dependent on sex steroid hormones, but specific growth factors are likely to play an important role in regulating this process. A number of cytokines and growth factors are synthesized in the endometrium in response to sex steroid hormones and act to regulate endometrial function. Endometrial cells produce **interleukin-8** (**IL-8**) both in vivo and in vitro. We hypothesized that **IL-8**, a neutrophil chemoattractant/activating factor and a potent angiogenic agent that has been shown to stimulate growth in other cell types, may directly stimulate proliferation of endometrial cells. We first investigated the effect of **IL-8** and mouse antihuman-**IL-8** neutralizing antibody on endometrial stromal cell proliferation using both a colorimetric assay and thymidine uptake. We then investigated the modulation of endometrial stromal cell **IL-8** production and proliferation by **antisense** oligonucleotides specific for **IL-8**. There was a concentration-dependent increase of cell proliferation with **IL-8** (2-fold at 1 ng/mL; $P < 0.01$ between control and concentrations above 0.01 ng/mL) and a concentration-dependent inhibition of cell proliferation with anti-**IL-8** antibody (to 30% of the control at 1 microg/mL; $P < 0.01$ between control and concentrations above 0.1 microg/mL). **IL-8 antisense** oligonucleotide treatment decreased **IL-8** production by endometrial stromal cells in culture as well as cell proliferation when it is compared with scrambled (nonsense) oligonucleotide treatment ($P < 0.01$). Addition of **IL-8** (1 ng/mL) reversed the proliferation **inhibitory** effect of **IL-8 antisense** oligonucleotides. We propose that **IL-8** may act as an autocrine growth factor in the endometrium, and suggest that it may also play a role in the pathogenesis of endometriosis.

L12 ANSWER 10 OF 48 MEDLINE
ACCESSION NUMBER: 1998182313 MEDLINE
DOCUMENT NUMBER: 98182313 PubMed ID: 9516148
TITLE: Mechanisms of growth control of Kaposi's sarcoma-associated herpes virus-associated primary effusion lymphoma cells.
AUTHOR: Asou H; Said J W; Yang R; Munker R; Park D J; Kamada N; Koeffler H P
CORPORATE SOURCE: Division of Hematology/Oncology and Pathology, Cedars-Sinai Medical Center, UCLA School of Medicine, Los Angeles, CA 90048, USA.
CONTRACT NUMBER: CA 42710 (NCI)
UO1 CA 66533-02 (NCI)
SOURCE: BLOOD, **(1998 Apr 1)** 91 (7) 2475-81.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199804

ENTRY DATE: Entered STN: 19980422
Last Updated on STN: 19980422
Entered Medline: 19980415

AB Primary effusion lymphoma (PEL) is a distinct clinicopathologic entity associated with Kaposi's sarcoma-associated herpes virus (KSHV). Several cytokines, including interleukin-6 (IL-6), basic fibroblast growth factor (bFGF), and platelet-derived growth factor (PDGF) may be important for survival of KS cells. However, little is known about the interaction of cytokines with KSHV-infected lymphocytes from PEL. Therefore, we investigated what cytokines were produced by KSHV-infected PEL cell lines (KS-1, BC-1, BC-2), what cytokine receptors were expressed by these cells, what response these cells had to selected cytokines, and what was the effect of IL-6 **antisense** phosphorothioated oligonucleotides. Reverse transcriptase-polymerase chain reaction (RT-PCR) and protein studies showed that these three cell lines produced IL-10, IL-6, and the receptors for IL-6. The granulocyte macrophage colony-stimulating factor (GM-CSF), **IL**-1beta, **IL-8**, **IL**-12, bFGF, PDGF, and c-kit transcripts were not detected in the cell lines. High levels (0.7 to 5 ng/mL/10(6) cells/48 hours) of IL-6 protein were consistently detected in supernatants of the cell lines by enzyme-linked immunosorbent assay (ELISA) tests. In clonogenic assays, interferon-alpha (IFN-alpha) and IFN-gamma suppressed the clonal growth of the PEL cells, but GM-CSF, IL-4, **IL**-6, **IL-8**, **IL**-10, and oncostatin M did not change it. We examined for several autocrine loops that have been suggested to occur in KS. Experiments using **antisense** oligonucleotides showed that the clonal growth of KS-1 and BC-1 was nearly 100% **inhibited** by IL-6 **antisense** oligonucleotides (10 micromol/L), but not at all by either oligonucleotides (</=10 micromol/L) to IL-6 sense, IL-6 scrambled, viral IL-6 (vIL-6) **antisense**, or IL-10 **antisense**. Furthermore, the IL-6 **antisense** oligonucleotides had no effect on two B-cell lymphoma cell lines, which were not infected with KSHV. Addition of IL-6 antibody did not inhibit clonal growth of any of the cell lines. Taken together, we have defined the cytokines and their receptors expressed on PEL cells and have found that these cells synthesized IL-6 and IL-6 receptors; interruption of this pathway by IL-6 **antisense** oligonucleotides specifically prevented the growth of these cells. These findings will offer potential new therapeutic strategies for PEL.

L12 ANSWER 11 OF 48 MEDLINE
ACCESSION NUMBER: 1998027997 MEDLINE
DOCUMENT NUMBER: 98027997 PubMed ID: 9361904
TITLE: Sequence-specific inhibition of the tumor necrosis factor-alpha receptor I gene by oligodeoxynucleotides containing N7 modified 2'-deoxyguanosine.
AUTHOR: Ojwang J O; Lewis A F; Revankar G R; Walker D; Akiyama T; Hogan M E; Rando R F
CORPORATE SOURCE: Aronex Pharmaceuticals, Inc., Woodlands, TX 77380, USA.
CONTRACT NUMBER: 5RO1AI32894 (NIAID)
SOURCE: ANTISENSE AND NUCLEIC ACID DRUG DEVELOPMENT, **(1997 Oct)** 7 (5) 447-59.
Journal code: 9606142. ISSN: 1087-2906.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971218

AB Tumor necrosis factor-alpha (TNF-alpha) is a highly pleiotropic cytokine produced mainly by activated macrophages. This cytokine has been found to

mediate the growth of certain tumors, the replication of HIV-1, septic shock, cachexia, graft-versus-host disease, and autoimmune diseases. The binding of TNF-alpha to the p55 tumor necrosis factor receptor type I (TNFRI) is considered one of the initial steps responsible for the multiple physiologic effects mediated by TNF-alpha. The role of TNF-alpha as an inflammatory mediator through TNFRI makes both of these genes attractive targets for intervention in both acute and chronic inflammatory diseases. We have designed **antisense** oligodeoxynucleotides (ODNs) containing chemically **modified** purine and pyrimidine bases that specifically inhibit TNFRI expression and functions. These ODNs were designed to hybridize to the 3'-polyadenylation signal region of the TNFRI gene. In cell-based assays, gene-specific **antisense inhibition** occurred in a dose-dependent fashion at submicromolar concentrations in the presence of cellular uptake enhancing agents. Within ODN sets with a common pattern of stabilizing backbone substitution, the inhibition of the gene expression is found to be correlated with the affinity of the ODNs for their cognate mRNA target sites, providing direct evidence for an **antisense** mechanism of action. In addition, events triggered by the binding of TNF-alpha to TNFRI, such as the production of IL-6 and **IL-8**, were significantly reduced by treatment of cells with the anti-TNFRI ODN. Therefore, **antisense** ODNs can be used to control biologic processes mediated by TNF-alpha and may be useful as therapeutic agents to treat conditions resulting from overproduction of TNF-alpha.

L12 ANSWER 12 OF 48 MEDLINE

ACCESSION NUMBER: 97342639 MEDLINE
DOCUMENT NUMBER: 97342639 PubMed ID: 9199336
TITLE: Involvement of **interleukin-8**, vascular endothelial growth factor, and basic fibroblast growth factor in tumor necrosis factor alpha-dependent angiogenesis.
AUTHOR: Yoshida S; Ono M; Shono T; Izumi H; Ishibashi T; Suzuki H; Kuwano M
CORPORATE SOURCE: Department of Biochemistry, Kyushu University School of Medicine, Fukuoka, Japan.
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, **(1997 Jul)** 17 (7) 4015-23.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970724

AB Tumor necrosis factor alpha (TNF-alpha) is a macrophage/monocyte-derived polypeptide which modulates the expression of various genes in vascular endothelial cells and induces angiogenesis. However, the underlying mechanism by which TNF-alpha mediates angiogenesis is not completely understood. In this study, we assessed whether TNF-alpha-induced angiogenesis is mediated through TNF-alpha itself or indirectly through other TNF-alpha-induced angiogenesis-promoting factors. Cellular mRNA levels of **interleukin-8** (**IL-8**), vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), and their receptors were increased after the treatment of human microvascular endothelial cells with TNF-alpha (100 U/ml). TNF-alpha-dependent tubular morphogenesis in vascular endothelial cells was inhibited by the administration of anti-**IL-8**, anti-VEGF, and anti-bFGF antibodies, and coadministration of all three antibodies almost completely abrogated tubular formation. Moreover,

treatment with Sp1, NF-kappaB, and c-Jun **antisense** oligonucleotides **inhibited** TNF-alpha-dependent tubular morphogenesis by microvascular endothelial cells. Administration of a NF-kappaB **antisense** oligonucleotide almost completely **inhibited** TNF-alpha-dependent **IL-8** production and partially abrogated TNF-alpha-dependent VEGF production, and an Sp1 **antisense** sequence partially **inhibited** TNF-alpha-dependent production of VEGF. A c-Jun **antisense** oligonucleotide significantly **inhibited** TNF-alpha-dependent bFGF production but did not affect the production of **IL-8** and VEGF. Administration of an anti-**IL-8** or anti-VEGF antibody also blocked TNF-alpha-induced neovascularization in the rabbit cornea in vivo. Thus, angiogenesis by TNF-alpha appears to be modulated through various angiogenic factors, both in vitro and in vivo, and this pathway is controlled through paracrine and/or autocrine mechanisms.

L12 ANSWER 13 OF 48 MEDLINE
ACCESSION NUMBER: 97309359 MEDLINE
DOCUMENT NUMBER: 97309359 PubMed ID: 9166774
TITLE: **Modified antisense** oligonucleotides directed against tumor necrosis factor receptor type I inhibit tumor necrosis factor alpha-mediated functions.
AUTHOR: Ojwang J O; Mustain S D; Marshall H B; Rao T S; Chaudhary N; Walker D A; Hogan M E; Akiyama T; Revankar G R; Peyman A; Uhlmann E; Rando R F
CORPORATE SOURCE: Aronex Pharmaceuticals, Inc., The Woodlands, Texas 77381-4223, USA.. jojwang@aronex.com
SOURCE: BIOCHEMISTRY, **(1997 May 20)** 36 (20) 6033-45. Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970709
Last Updated on STN: 19970709
Entered Medline: 19970623

AB Tumor necrosis factor alpha (TNF alpha), a polypeptide produced by activated macrophages, is a highly pleiotropic cytokine which elicits inflammatory and immunological reactions. The binding of TNF alpha to tumor necrosis factor receptor type I (TNFRI) is considered the initial step responsible for some of the multiple biological functions mediated by TNF alpha. The role of TNF alpha as an inflammatory mediator through human TNFRI makes TNFRI an attractive target for intervention, in both acute and chronic inflammatory diseases. In this study, we have identified partial phosphorothioate oligodeoxyribonucleotides (ODNs) containing C-5 propynyl or hexynyl derivatives of 2'-deoxyuridine which specifically inhibited TNFRI and subsequently inhibited the functions of TNF alpha mediated through TNFRI. The most active ODNs were directed against the 3'-poly adenylation signal site on the TNFRI mRNA, and in a cellular assay, gene-specific **antisense inhibition** occurred in a dose-dependent fashion at submicromolar concentrations, in the presence of Cellfectin. The inhibition of gene expression correlated with the binding affinity of the ODN for the target mRNA. The ODNs lowered TNFRI protein levels and TNF alpha-mediated functions by specifically reducing levels of TNFRI mRNA. These anti-TNFRI ODNs offer a novel approach for controlling biological functions of TNF alpha and may be useful as human therapeutic agents for treating diseases in which TNF alpha has been implicated.

L12 ANSWER 14 OF 48 MEDLINE
ACCESSION NUMBER: 97307623 MEDLINE
DOCUMENT NUMBER: 97307623 PubMed ID: 9164965

TITLE: Thrombin induces endothelial type II activation in vitro: IL-1 and TNF-alpha-independent **IL-8** secretion and E-selectin expression.
AUTHOR: Kaplanski G; Fabrigoule M; Boulay V; Dinarello C A; Bongrand P; Kaplanski S; Farnarier C
CORPORATE SOURCE: Laboratory of Immunology, INSERM Unit 387, Hospital Sainte Marguerite, Marseille, France.
CONTRACT NUMBER: NIH 15614
SOURCE: JOURNAL OF IMMUNOLOGY, **(1997 Jun 1)** 158 (11) 5435-41.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970630
Last Updated on STN: 19970630
Entered Medline: 19970619

AB In addition to its role in coagulation, thrombin is involved in the inflammatory process by inducing vessel neutrophilic infiltration. Thrombin induces endothelial P-selectin expression and platelet activating factor release, which participate to induce early neutrophil adhesion and activation. We employed HUVEC and now show that thrombin induces the production of the chemokine **IL-8** in a time- and dose-dependent fashion. Similarly, thrombin induced E-selectin expression on HUVEC. Both **IL-8** secretion and E-selectin expression were preceded by an increase in steady state levels of the respective mRNAs. Thrombin action on HUVEC was inhibited by the specific thrombin inhibitor, hirudin. In addition, these effects of thrombin on HUVEC were mimicked by the 14-amino acid thrombin receptor agonist peptide, which triggers the native thrombin receptor in a similar fashion to thrombin itself. Although IL-1 and TNF-alpha also induce **IL-8** and E-selectin, the thrombin effects in these experiments were not mediated by those cytokines, since neither IL-1 receptor antagonist nor anti-TNF-alpha Ab inhibited the effects of thrombin. Furthermore, IL-1alpha, IL-1beta, and TNF-alpha were not detected in the supernatants of thrombin-activated HUVEC. Although intracellular IL-1alpha was found in thrombin-activated HUVEC, **antisense** IL-1alpha had no **inhibitory** effect on **IL-8** secretion. These results demonstrate that in addition to short term endothelial activation, thrombin also functions as a long acting proinflammatory agent by inducing endothelial synthesis of the mediators required for neutrophils activation and extravazation during inflammation.

L12 ANSWER 15 OF 48 MEDLINE
ACCESSION NUMBER: 97194778 MEDLINE
DOCUMENT NUMBER: 97194778 PubMed ID: 9042216
TITLE: Reversible inhibition of **IL-8** receptor B mRNA expression and proliferation in non-small cell lung cancer by **antisense** oligonucleotides.
AUTHOR: Olbina G; Cieslak D; Ruzdijic S; Esler C; An Z; Wang X; Hoffman R; Seifert W; Pietrzkowski Z
CORPORATE SOURCE: Research Department, ICN Pharmaceuticals, Inc., Costa Mesa, CA 92626, USA.
SOURCE: ANTICANCER RESEARCH, **(1996 Nov-Dec)** 16 (6B) 3525-30.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970407
Last Updated on STN: 19970407
Entered Medline: 19970327

AB We examined the importance of **IL-8** receptor B mRNA expression in the growth of non-small cell lung cancer (NSCLC). Using **antisense** oligonucleotide ICN 197, we were able to inhibit **IL-8** R B mRNA expression in vitro. The sequence specific effect of **antisense** oligonucleotide and down-**regulation** of **IL-8** R B mRNA was shown by Reverse Transcription Polymerase Chain Reaction (RT-PCR) and Southern blot analysis. The proliferation of treated cells was measured by 3H thymidine incorporation. We found that treatment of NSCLC cells caused reversible growth inhibition and reversible down regulation of **IL-8** R B mRNA. Furthermore, we observed that the treatment of nude mice with oligonucleotide ICN 197 inhibited the growth of tumors developed from NSCLC cells injected subcutaneously. Our data in vitro suggest that **IL-8** receptor B mRNA expression is required to maintain the proliferative rate of NSCLC. Based on the data in vivo. oligonucleotide ICN 197 may be considered for the development of novel therapeutic treatment for lung cancer.

L12 ANSWER 16 OF 48 MEDLINE
ACCESSION NUMBER: 96315649 MEDLINE
DOCUMENT NUMBER: 96315649 PubMed ID: 8754823
TITLE: Involvement of the transcription factor NF-kappaB in tubular morphogenesis of human microvascular endothelial cells by oxidative stress.
AUTHOR: Shono T; Ono M; Izumi H; Jimi S I; Matsushima K; Okamoto T; Kohno K; Kuwano M
CORPORATE SOURCE: Department of Biochemistry, Kyushu Unviersity School of Medicine, Fukuoka, Japan.
CONTRACT NUMBER: CA-14195 (NCI)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, **(1996 Aug)** 16 (8) 4231-9.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19961008
Last Updated on STN: 19961008
Entered Medline: 19960920

AB Oxygen radicals are induced under various pathologic conditions associated with neovascularization. Oxygen radicals modulate angiogenesis in cultured human microvascular endothelial cells by an unknown mechanism. Treatment of human microvascular endothelial cells for 15 min with 0.1 to 0.5 mM hydrogen peroxide (H2O2) or 100 U of tumor necrosis factor alpha per ml induced tubular morphogenesis in type I collagen gels. Gel shift assays with nuclear extracts demonstrated that H2O2 increases the binding activities of two transcription factors, NF-kappaB and AP-1, but not of Spl. Tumor necrosis factor alpha increased the binding activities of all three factors. A supershift assay with specific antibodies against JunB, JunD, and c-Jun (Jun family) showed that the antibody against c-Jun supershifted the AP-1 complex after H2O2 treatment. Coadministration of the **antisense** sequence of NF-kappaB **inhibited** H2O2-dependent tubular morphogenesis, and the **antisense** c-Jun oligonucleotide caused partial **inhibition**. The angiogenic factor responsible for H2O2-induced tubular morphogenesis was examined. Cellular mRNA levels of vascular endothelial growth factor and **interleukin -8** (**IL-8**), but not those of transforming

growth factor alpha, were increased after treatment with 0.5 mM H2O2. Coadministration of anti-**IL-8** antibody inhibited tubular morphogenesis enhanced by H2O2, and **IL-8** itself also enhanced the formation of tube-like structures. Treatment with **antisense** NF-kappaB oligonucleotide completely blocked H2O2-dependent **IL-8** production by endothelial cells. The tubular morphogenesis of vascular endothelial cells after treatment with oxidative stimuli and its possible association with NF-kappaB and **IL-8**, is examined.

L12 ANSWER 17 OF 48 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:341676 BIOSIS
DOCUMENT NUMBER: PREV200000341676
TITLE: **Inhibition** of tumor growth by **antisense** oligonucleotides for **IL-8** and **IL-8** receptor.
AUTHOR(S): Pietrzkowski, Zbigniew (1); Cieslak, Dariusz; Olbina, Gordan
CORPORATE SOURCE: (1) Foothill Ranch, CA USA
ASSIGNEE: IGN Pharmaceuticals, Inc., Costa Mesa, CA, USA
PATENT INFORMATION: US 6017898 January 25, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (**Jan. 25, 2000**) Vol. 1230, No. 4, pp. No pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Oligonucleotides are provided which are effective in inhibiting the growth, metastasis and/or angiogenesis of tumors, including particularly melanoma and/or lung cancer. Methods are also provided for use of these oligonucleotides in the treatment of diseases.

L12 ANSWER 18 OF 48 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95147778 EMBASE
DOCUMENT NUMBER: 1995147778
TITLE: Immunomodulation by cytokine **antisense** oligonucleotides.
AUTHOR: D'Hellencourt C.L.; Diaw L.; Guenounou M.
CORPORATE SOURCE: Laboratoire Biologie des Cytokines, C.H.R. Robert Debre, rue Alexis Carrel,51092 Reims cedex, France
SOURCE: European Cytokine Network, (1995) 6/1 (7-19).
ISSN: 1148-5493 CODEN: ECYNEJ
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The cytokine network is involved in normal immune reaction and in the progression of several pathologies. **Antisense** (AS) oligonucleotides, which allow specific **inhibition** of expression of proteins, offer a new methodology to investigate this complex network. This review focuses on the use of AS to modulate cytokine expression. AS may act in different ways such as blocking fixation or progression of the ribosome along the mRNA, mRNA cleavage by RNase H, or preventing normal RNA maturation. In order to improve AS efficiency, chemical modifications have been developed, and improvement of oligonucleotide uptake has been achieved with different systems of vectorization including liposomes (neutral, cationic, immunoliposome), nanoparticles, or covalent attachment of a carrier, In oncogenesis, intracellular or extracellular autocrine

loops have been demonstrated by the use of cytokine AS. Involvement of cytokines in immunological reactions (TH1 and TH2 subset, IgE response, lymphokine activated killer, cytotoxic T lymphocyte...) and in hematopoiesis have also been studied with this approach. Therapeutic application of AS has been suggested by inhibition of inflammatory cytokines in vivo. Clinical trials using AS are under investigation in virological and in oncological diseases. At present, cytokine **antisenses** primarily represent a tool for dissecting the function of a cytokine in vitro, but they may offer in the future a new way for immunomodulation intervention,

L12 ANSWER 19 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:293220 CA
TITLE: Adenoviral-mediated gene therapy of human bladder cancer with **antisense interleukin-8**
AUTHOR(S): Inoue, Keiji; Wood, Christopher G.; Slaton, Joel W.; Karashima, Takashi; Sweeney, Paul; Dinney, Colin P. N.
CORPORATE SOURCE: Department of Cancer Biology, The University of Texas M.D Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Oncology Reports (**2001**), 8(5), 955-964
CODEN: OCRPEW; ISSN: 1021-335X
PUBLISHER: Oncology Reports
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We previously demonstrated the importance of **interleukin-8** (**IL-8**) as a mediator of angiogenesis, tumorigenicity, and metastasis of transitional cell carcinoma (TCC) of the bladder. In the present study, we evaluated the feasibility of adenoviral mediated **antisense IL-8** gene transfer (Ad **IL-8**-AS) as therapy for established TCC. In vitro, Ad **IL-8**-AS inhibited endothelial cell proliferation and enhanced endothelial cell apoptosis. The highly metastatic human TCC cell line 253J B-VR was implanted into the subcutis of athymic nude mice, and intralesional therapy with Ad **IL-8**-AS commenced when the tumors reached a diam. between 5 and 7 mm. Tumor growth was significantly inhibited compared with therapy in controls (saline and ss-galactosidase adenovirus). Ad **IL-8**-AS therapy decreased the in vivo expression of **IL-8** and matrix metalloproteinase type 9 (MMP-9), reduced microvessel d., and enhanced endothelial cell apoptosis. These results indicate that Ad **IL-8**-AS therapy targets both tumor cells and host endothelial cells resulting in endothelial cell apoptosis and significant inhibition of tumor growth.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 20 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:117140 CA
TITLE: Regulation of hematopoietic growth factor production by genetically modified human bone marrow stromal cells expressing interleukin-1.beta. **antisense** RNA
AUTHOR(S): Hartwig, Udo F.; Keller, Ulrich; Huber, Christoph; Peschel, Christian
CORPORATE SOURCE: III. Department of Medicine, Johannes-Gutenberg University Mainz, Mainz, Germany
SOURCE: Journal of Interferon and Cytokine Research ( **2001**), 21(10), 851-860
CODEN: JICRFJ; ISSN: 1079-9907
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Interleukin-1 (IL-1) plays a major role in the regulation of bone marrow stromal cell function and hematopoiesis. It is known to induce secretion of the hematopoietic growth factors granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage CSF (GM-CSF), IL-6, and **IL-8** as well as IL-1 itself in stromal cells. We investigated the role of IL-1.beta.-mediated growth factor prodn. in the human stromal cell line L88/5. Using liposome-mediated DNA transfer, two stromal cell transfectants that constitutively express IL-1.beta. **antisense** (AS) RNA were generated. Expression of IL-1.beta. AS RNA and IL-1.beta. RNA was detd. by RT-PCR. The stromal cell transfectants were strongly impaired in their endogenous IL-1.beta. prodn., and this effect was present even when strong IL-1.beta. inducers, such as IL-1.alpha. and tumor necrosis factor-.alpha. (TNF-.alpha.), were used. Reduced endogenous IL-1.beta. levels had no effect on the constitutive prodn. of **IL-6**, **IL-8**, and GM-CSF measured by ELISA. In contrast to lipopolysaccharide (LPS) stimulation, IL-1.alpha.-mediated stimulation of GM-CSF prodn. was significantly reduced in AS transfectants. TNF-.alpha. induced GM-CSF prodn. was also reduced. IL-6 and **IL-8** prodn. was increased in transfectants, suggesting a neg. regulatory role of IL-1.beta. in L88/5. This new approach using AS technol. to specifically target constitutive RNA expression will allow further characterization of the bone marrow cytokine network in normal and malignant hematopoiesis.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 21 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:308839 CA
TITLE: Genetically modified lung cancer cells expressing a TGF-.beta. inhibitor for antitumor application
INVENTOR(S): Fakhrai, Habib
PATENT ASSIGNEE(S): Novarx, USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001074404 | A2 | 20011011 | WO 2001-US10339 | 20010330 <-- |
| WO 2001074404 | A3 | 20021017 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| EP 1267945 | A2 | 20030102 | EP 2001-926498 | 20010330 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2000-193497P P 20000331
WO 2001-US10339 W 20010330

AB The present invention relates to compns. comprising a therapeutically effective amt. of genetically modified cells contg. a genetic construct expressing a TGF.beta. inhibitor effective to reduce expression of

TGF.beta., where the genetically modified cells are non-small cell lung cancer (NSCLC) cells or small cell lung cancer (SCLC) cells, and related methods.

L12 ANSWER 22 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:252790 CA
TITLE: Single nucleotide polymorphisms in human genes
INVENTOR(S): Cargill, Michele; Ireland, James S.; Lander, Eric S.
PATENT ASSIGNEE(S): Whitehead Institute for Biomedical Research, USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001066800 | A2 | 20010913 | WO 2001-US7268 | 20010307 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2002032319 | A1 | 20020314 | US 2001-801274 | 20010307 |
| PRIORITY APPLN. INFO.: | | | US 2000-187510P P | 20000307 |
| | | | US 2000-206129P P | 20000522 |

AB The invention provides nucleic acid segments of the human genome, particularly nucleic acid segments from genes including polymorphic sites. The polymorphisms were identified by resequencing of target sequences from individuals of diverse ethnic and geog. backgrounds by hybridization to probes immobilized to microfabricated arrays. Some of the single nucleotide polymorphisms (SNPs) specify a different amino acid sequence, some are silent or are in noncoding regions, and some specify a stop signal in protein translation. Allele-specific primers and probes hybridizing to regions flanking or contg. these sites are also provided. The nucleic acids, primers and probes are used in applications such as phenotype correlations, forensics, paternity testing, medicine and genetic anal.

L12 ANSWER 23 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:163432 CA
TITLE: cDNA encoding human and mouse interleukin 17 receptor-related protein EVI27
INVENTOR(S): Shaughnessy, John D.
PATENT ASSIGNEE(S): Board of Trustees of the University of Arkansas, USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001057202 | A2 | 20010809 | WO 2001-US3518 | 20010202 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, | | | | |

KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002102639 A1 20020801 US 2001-778971 20010202
PRIORITY APPLN. INFO.: US 2000-180374P P 20000204

AB The invention relates to cDNA encoding human and mouse interleukin 17 receptor-related protein EVI27 which expression is upregulated by viral integration at Evi27 locus. The invention relates to human chromosomal mapping of Evi27 gene which was identified to be located at chromosome 3p21 by fluorescence in situ hybridization of high-resoln. G-banded chromosomes. The invention also relates to expression and subcellular location of protein Evi27.

L12 ANSWER 24 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:361373 CA
TITLE: Protein kinase inhibitors and other agents for the treatment of Helicobacter pylori-induced gastrointestinal diseases
INVENTOR(S): Wallasch, Christian; Bevec, Dorian
PATENT ASSIGNEE(S): Axxima Pharmaceuticals A.-G., Germany
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| WO 2001035899 | A2 | 20010525 | WO 2000-EP11444 | 20001117 | <-- |
| WO 2001035899 | A3 | 20011213 | | | |
| WO 2001035899 | C2 | 20020919 | | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| AU 2001030037 | A5 | 20010530 | AU 2001-30037 | 20001117 | <-- |
| EP 1229925 | A2 | 20020814 | EP 2000-990605 | 20001117 | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:
EP 1999-123042 A 19991119
US 1999-448013 A 19991123
WO 2000-EP11444 W 20001117

AB A method is disclosed for the manuf. of a medicament for treating or preventing Helicobacter mediated diseases in a mammal and a method for treating or preventing Helicobacter-mediated diseases. The compds. of the invention include CCK-B inhibitors, protein kinase C inhibitors, membrane-assocd. metalloproteinase inhibitors, growth factor receptor activation inhibitors, growth factor receptor kinase inhibitors, mitogen-activated protein kinase cascade inhibitors, and transcription inhibitors.

L12 ANSWER 25 OF 48 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 134:324369 CA
TITLE: Production of experimental malignant pleural effusions is dependent on invasion of the pleura and expression of vascular endothelial growth factor/vascular permeability factor by human lung cancer cells
AUTHOR(S): Yano, Seiji; Shinohara, Hisashi; Herbst, Roy S.; Kuniyasu, Hiroki; Bucana, Corazon D.; Ellis, Lee M.; Fidler, Isaiah J.
CORPORATE SOURCE: Department of Cancer Biology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: American Journal of Pathology (**2000**), 157(6), 1893-1903
CODEN: AJPAA4; ISSN: 0002-9440
PUBLISHER: American Society for Investigative Pathology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We detd. the mol. mechanisms that regulate the pathogenesis of malignant pleural effusion (PE) assocd. with advanced stage of human, non-small-cell lung cancer. I.v. injection of human PC14 and PC14PE6 (adenocarcinoma) or H226 (squamous cell carcinoma) cells into nude mice yielded numerous lung lesions. PC14 and PC14PE6 lung lesions invaded the pleura and produced PE contg. a high level of vascular endothelial growth factor (VEGF)-localized vascular hyperpermeability. Lung lesions produced by H226 cells were confined to the lung parenchyma with no PE. The level of expression of VEGF mRNA and protein by the cell lines directly correlated with extent of PE formation. Transfection of PC14PE6 cells with **antisense** VEGF165 gene did not **inhibit** invasion into the pleural space but reduced PE formation. H226 cells transfected with either sense VEGF 165 or sense VEGF 121 genes induced localized vascular hyperpermeability and produced PE only after direct implantation into the thoracic cavity. The prodn. of PE was thus assocd. with the ability of tumor cells to invade the pleura, a property assocd. with expression of high levels of urokinase-type plasminogen activator and low levels of TIMP-2. Collectively, the data demonstrate that the prodn. of malignant PE requires tumor cells to invade the pleura and express high levels of VEGF/VPF.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 26 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:322353 CA
TITLE: Post-translational modification of recombinant proteins in plants by altering its natural modification abilities
INVENTOR(S): Russell, Douglas; Manjunath, Siva; Bassuner, Ronald
PATENT ASSIGNEE(S): Monsanto Company, USA
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001029242 | A2 | 20010426 | WO 2000-US29027 | 20001020 <-- |
| WO 2001029242 | A3 | 20020221 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,

ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1224309 A2 20020724 EP 2000-978257 20001020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: US 1999-160758P P 19991021
US 2000-195282P P 20000407
WO 2000-US29027 W 20001020

AB The present invention is directed to methods for producing a post-translationally modified heterologous polypeptide in a plant host system by altering the natural post-translational abilities of that plant host system. The post-translational modification may be proteolytic cleavage, glycosylation, phosphorylation,methylation, sulfation, prenylation, acetylation, N-amidation, oxidn., hydroxylation, or myristylation. In a preferred embodiment, this method includes transforming a plant host system with a nucleic acid that encodes a heterologous polypeptide, and isolating that polypeptide from the plant host system. The heterologous proteins may include antibodies and antibody fragments, collagen types I-XX, human protein C, and cytokines. In another aspect of this method, altering the natural post-translational modifications is done by transforming the plant host system with one or more nucleic acid sequences encoding a post-translational modification enzyme. Such plant specific post-translational modifying enzymes include Galactosyl transferase, xylosyl transferase, and fucosyl transferase. In an alternative aspect, the altering is done by mutagenesis of plant host system. In another embodiment, the altering is done by transforming said plant host system with an expression vector comprising a nucleic acid sequence that encodes an **antisense** nucleic acid. The invention further provides a method for producing a post-translationally modified heterologous polypeptide in a plant host system, by cross-pollinating a first plant, wherein the plant has been transformed with a first expression vector comprising a nucleic acid sequence encoding a heterologous polypeptide, and a second plant wherein the second plant has been transformed with a second expression vector comprising a nucleic acid sequence encoding a post-translational modifying enzyme.

L12 ANSWER 27 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:141771 CA
TITLE: Methods using PPAR.delta. inhibitors for treatment of vascular diseases, cancer, Alzheimer's disease, and inflammatory disorders, and drug screening methods
INVENTOR(S): Palmer, Colin Neil Alexander; Vosper, Helen; Wolf, Charles Roland
PATENT ASSIGNEE(S): The University of Dundee, UK
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001007066 | A2 | 20010201 | WO 2000-EP6986 | 20000719 <-- |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| BR 2000012661 | A | 20020409 | BR 2000-12661 | 20000719 |
| EP 1200114 | A2 | 20020502 | EP 2000-956238 | 20000719 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003505058 | T2 | 20030212 | JP 2001-511949 | 20000719 |
| NO 2002000326 | A | 20020320 | NO 2002-326 | 20020122 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| GB 1999-17405 | A | 19990723 |
| WO 2000-EP6986 | W | 20000719 |

AB A method of preventing or reducing foam cell development from macrophages, or removing foam cells, in a patient comprises administering an effective amt. of an inhibitor of PPAR.delta. activity. A method of preventing or treating a vascular disease assocd. with plaque formation and/or thrombotic blockage of the blood vessels in a patient comprises administering to the patient an effective amt. of an inhibitor of PPAR.delta. activity. Also disclosed are methods for the treatment of cancer, Alzheimer's disease, and inflammatory disorders.

L12 ANSWER 28 OF 48 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 134:80833 CA

TITLE: Antisense method for the prophylaxis and/or treatment of psoriasis and other skin disorders

INVENTOR(S): Wraight, Christopher John; Werther, George Arthur; Edmondson, Stephanie Ruth

PATENT ASSIGNEE(S): Murdoch Childrens Research Institute, Australia

SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000078341 | A1 | 20001228 | WO 2000-AU693 | 20000621 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1191941 | A1 | 20020403 | EP 2000-936560 | 20000621 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2003502383 | T2 | 20030121 | JP 2001-504403 | 20000621 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1999-140345P | P | 19990621 |
| WO 2000-AU693 | W | 20000621 |

AB The present invention relates generally to a method for the prophylaxis and/or treatment of skin disorders, and in particular proliferative and/or inflammatory skin disorders, and to genetic mols. useful for same. The present invention is particularly directed to genetic mols. capable of modulating growth factor interaction with its receptor on epidermal keratinocytes to inhibit, reduce or otherwise decrease stimulation of this layer of cells. The present invention contemplates, in a most preferred embodiment, a method for the prophylaxis and/or treatment of psoriasis.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 29 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:329593 CA
TITLE: Low adenosine anti-sense oligonucleotide, compositions, kit and method for treatment of airway disorders associated with bronchoconstriction, lung inflammation, allergy(ies) and surfactant depletion
INVENTOR(S): Nyce, Jonathan W.
PATENT ASSIGNEE(S): East Carolina University, USA
SOURCE: PCT Int. Appl., 1592 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000062736 | A2 | 20001026 | WO 2000-US8020 | 20000324 |
| WO 2000062736 | A3 | 20011011 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2000006019 | A | 20010313 | BR 2000-6019 | 20000324 |
| EP 1168919 | A2 | 20020109 | EP 2000-919668 | 20000324 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

PRIORITY APPLN. INFO.: US 1999-127958P P 19990406
WO 2000-US8020 W 20000324
OTHER SOURCE(S): MARPAT 133:329593

AB An in vivo method of selectively delivering a nucleic acid to a target gene or mRNA, comprises the topical administration, e.g. to the respiratory system, of a subject of a therapeutic amt. of an oligonucleotide (oligo) that is antisense to the initiation codon region, the coding region, the 5' or 3' intron-exon junctions or regions within 2 to 10 nucleotides of the junctions of the gene or antisense to a mRNA complementary to the gene in an amt. effective to reach the target polynucleotide and reducing or inhibiting expression. In addn. a method of treating an adenosine-mediated effect comprises topically administering to a subject an antisense oligo in an amt. effective to treat the respiratory, pulmonary, or airway disease. In order to minimize triggering adenosine receptors by their metab., the administered oligos have a low content of or are essentially free of adenosine. A pharmaceutical compn. and formulations comprise the oligo antisense to an adenosine receptor, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixts. Various formulations contain a requisite carrier, and optionally other additives and biol. active agents. The low-adenosine or adenosine-free (des-A) agent for practicing the method of the invention may be prepd. by selecting a target gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) assocd. with a disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60 % free of thymidine

(T) and synthesizing one or more anti-sense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepd. by selection of target nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the antisense oligonucleotides with a "Universal or alternative base". The agent, compn. and formulations are used for prophylactic, preventive and therapeutic treatment of ailments assocd. with impaired respiration, lung allergy(ies) and/or inflammation and depletion lung surfactant or surfactant hypoprodn., such as pulmonary vasoconstriction, inflammation, allergies, allergic rhinitis, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction. The present treatment is suitable for administration in combination with other treatments, e.g. before, during and after other treatments, including radiation, chemotherapy, antibody therapy and surgery, among others. Alternatively, the present agent is effectively administered prophylactically or therapeutically by itself for conditions without known therapies or as a substitute for therapies exhibiting undesirable side effects. The treatment of this invention may be administered directly into the respiratory system of a subject so that the agent has direct access to the lungs, or by other effective routes of administration, e.g. topically, transdermally, by implantation, etc., in an amt. effective to reduce or inhibit the symptoms of the ailment.

L12 ANSWER 30 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:203144 CA
TITLE: Low-adenosine antisense oligonucleotide agents, compositions, kits and treatments for respiratory disorders
INVENTOR(S): Nyce, Jonathan W.
PATENT ASSIGNEE(S): East Carolina University, USA
SOURCE: PCT Int. Appl., 1343 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000009525 | A2 | 20000224 | WO 1999-US17712 | 19990803 |
| WO 2000009525 | A3 | 20000518 | | |
| W: AU, CA, CN, MX, RU, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2333901 | AA | 20000224 | CA 1999-2333901 | 19990803 |
| AU 9953374 | A1 | 20000306 | AU 1999-53374 | 19990803 |
| EP 1102786 | A2 | 20010530 | EP 1999-939006 | 19990803 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |

PRIORITY APPLN. INFO.: US 1998-95212P P 19980803
WO 1999-US17712 W 19990803
OTHER SOURCE(S): MARPAT 132:203144

AB A compn. comprises a nucleic acid comprising an oligo antisense to a target such as polypeptide(s) assocd. with an ailment afflicting lung airways, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixts. Various formulations contain a requisite carrier, and optionally other additives and biol. active agents. The agent of the invention may be prepd. by selecting a target gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) assocd. with a disease(s) or condition(s)

afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60% free of thymidine (T) and synthesizing one or more antisense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepd. by selection of target nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the antisense oligonucleotides with a universal base. The agent, compn. and formulations are used for prophylactic, preventive and therapeutic treatment of ailments assocd. with impaired respiration, allergy(ies) and/or inflammation, such as pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction, pulmonary hypertension and bronchoconstriction, chronic bronchitis, emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), ischemic conditions including ischemia itself, and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. colon cancer, breast cancer, pancreatic cancer, lung cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic metastasis, etc., as well as all types of cancers with may metastasize or have metastasized to the lung(s), including breast and prostate cancer. The present treatment is suitable for administration in combination with other treatments, e.g. before, during and after other treatments, including radiation, chemotherapy, antibody therapy and surgery, among others. The present agent is effectively administered preventatively, prophylactically or therapeutically by itself for conditions without known therapies, or as a substitute for, or in conjunction with, other therapies exhibiting undesirable side effects. The treatment of this invention may be administered directly into the respiratory system of a subject, so that the agent has direct access to the airways and the lungs. The invention is exemplified with specificity and pharmacokinetic studies using phosphorothioated antisense oligonucleotides targeted to the adenosine receptors A1, A2a, A2b, and A3.

L12 ANSWER 31 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:131881 CA
TITLE: Tubular morphogenesis by genotoxic therapeutic agents that induce NF-.kappa.B activation in human vascular endothelial cells
AUTHOR(S): Goto, Daisuke; Izumi, Hiroto; Ono, Mayumi; Okamoto, Takeshi; Kohno, Kimitoshi; Kuwano, Michihiko
CORPORATE SOURCE: Department of Biochemistry, Kyushu University School of Medicine, Fukuoka, 812-82, Japan
SOURCE: Angiogenesis (**1999**), Volume Date 1998-1999, 2(4), 345-356
CODEN: AGIOFT; ISSN: 0969-6970
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Angiogenic stimuli induce tubular morphogenesis and angiogenesis in vascular endothelial cells, but these cells are highly vulnerable to cytokines, oxidative stress, and genotoxic anticancer agents. A transcription factor, NF-.kappa.B, is involved in the protection against apoptosis and in angiogenesis in response to stimuli that could induce cell death. NF-.kappa.B was specifically activated by the genotoxic anticancer therapeutic agents etoposide and doxorubicin, but not by bleomycin, mitomycin C and cisplatin, in human vascular endothelial cells in three independent assay systems: nuclear translocation of NF-.kappa.B, binding of NF-.kappa.B to its consensus sequence, and NF-.kappa.B -dependent transcription. Exposure to etoposide and doxorubicin induced tubular morphogenesis by vascular endothelial cells in type I collagen gel

at rates comparable to tumor necrosis factor-.alpha.. Co-administration of NF-.kappa.B **antisense** oligonucleotides **inhibited** the angiogenesis by doxorubicin and etoposide. In contrast, bleomycin, mitomycin C, and cisplatin did not induce angiogenesis. An angiogenic factor, **interleukin 8**, was dramatically induced in vascular endothelial cells treated with doxorubicin, but not in cells treated with cisplatin. Co-administration of anti-**interleukin 8** antibody almost completely blocked the doxorubicin-induced angiogenesis in vitro, suggesting a paracrine/autocrine control through drug-induced angiogenic factor(s). The presence or absence of NF-.kappa.B activation may have an essential role in tubular morphogenesis by vascular endothelial cells during chemotherapeutic treatment, possibly through **interleukin 8**.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 32 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:97615 CA
TITLE: NF.kappa.B activity inhibitors
INVENTOR(S): Baba, Masanori; Ono, Minoru
PATENT ASSIGNEE(S): Kaken Drug Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 11180873 | A2 | 19990706 | JP 1997-353879 | 19971222 <-- |
| EP 931544 | A2 | 19990728 | EP 1998-104269 | 19980310 <-- |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: JP 1997-353879 19971222

AB Alkaloids [e.g. cepharanthin and isotetrandrine] isolated from Stephania cepharantha are nuclear factor .kappa.B activity inhibitors useful for prophylactic or therapeutic use.

L12 ANSWER 33 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:49447 CA
TITLE: Inhibition of tumor growth by inhibiting macrophage angiogenic activity
INVENTOR(S): Bourdon, Mario A.; Deryugina, Elena; Rao, Pothapragada Srirama; Borgstrom, Per
PATENT ASSIGNEE(S): La Jolla Institute for Experimental Medicine, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9929345 | A1 | 19990617 | WO 1998-US25791 | 19981204 <-- |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,

FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9918044 A1 19990628 AU 1999-18044 19981204 <--

PRIORITY APPLN. INFO.: US 1997-67591P P 19971205
WO 1998-US25791 W 19981204

AB Methods of inhibiting tumor growth in a mammalian host are provided. In the subject methods, the angiogenic activity of macrophages in at least the region of the tumor is inhibited, conveniently by providing an environment free of activated macrophages in at least the region of the tumor. The environment free of activated macrophages may be provided by depleting at least the region of the tumor of macrophages and/or inhibiting macrophage activation. The subject methods find use in cancer therapy and may be used in combination with one or more addnl. cancer treatment modalities, including surgery, radiation therapy and chemotherapy.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 34 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:306599 CA
TITLE: Antisense oligonucleotides capable of binding to multiple targets and their use in the treatment of respiratory disease
INVENTOR(S): Nyce, Jonathan W.
PATENT ASSIGNEE(S): East Carolina University, USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9913886 | A1 | 19990325 | WO 1998-US19419 | 19980917 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2304312 | AA | 19990325 | CA 1998-2304312 | 19980917 |
| AU 9893951 | A1 | 19990405 | AU 1998-93951 | 19980917 |
| AU 752531 | B2 | 20020919 | | |
| EP 1019065 | A1 | 20000719 | EP 1998-947089 | 19980917 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| BR 9812650 | A | 20000822 | BR 1998-12650 | 19980917 |

PRIORITY APPLN. INFO.: US 1997-59160P P 19970917
US 1998-93972 A 19980609
WO 1998-US19419 W 19980917

AB Antisense oligonucleotides carrying sequences that will allow them to bind to more than one mRNA in a target cell are described. Such oligonucleotides can be used as a single treatment for diseases having more than one contributing pathway. In particular, oligonucleotides effective against genes involved in the etiol. of respiratory disease are targeted. Preferably, the oligonucleotides are low in adenosine (.ltoreq.15%) and may have adenosines substituted with analogs. These oligonucleotides are targeted to high (G+C) sequences within mRNAs. Thus, phosphorothioate antisense oligonucleotide (HAdA1AS, 5'-gatggagggcggcatggcggg-3') designed for the adenosine A1 receptor is

provided. HAdA1AS significantly and specifically reduces the in vivo response to adenosine challenge in a dose-dependent manner, is effective in protection against aeroallergen-induced bronchoconstriction (house dust mite), has an unexpected long-term duration of effect (8.3 days for both PC50 adenosine and resistance), and is free of side effects that might be toxic to the recipient. Such oligonucleotides may be used for treating a disease or condition assocd. with lung airway, such as bronchoconstriction, inflammation, or allergies.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 35 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:61063 CA
TITLE: **Antisense** oligonucleotides for **IL-8** and **IL-8** receptor, and use in treatment of cancer
INVENTOR(S): Pietrzkowski, Zbigniew; Cieslak, Dariusz; Olbina, Gordana
PATENT ASSIGNEE(S): ICN Pharmaceuticals, Inc., USA
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 561,302, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5849903 | A | 19981215 | US 1997-796031 | 19970205 <-- |
| CA 2236825 | AA | 19970529 | CA 1996-2236825 | 19961116 <-- |
| CN 1202900 | A | 19981223 | CN 1996-198451 | 19961116 <-- |
| US 6017898 | A | 20000125 | US 1998-55913 | 19980406 <-- |

PRIORITY APPLN. INFO.: US 1995-561302 B2 19951121
US 1997-796031 A3 19970205

AB Oligonucleotides are provided which are effective in inhibiting the growth, metastasis and/or angiogenesis of tumors, including particularly melanoma and/or lung cancer. Methods are also provided for use of these oligonucleotides in the treatment of diseases.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 36 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:104207 CA
TITLE: Osteonectin inhibitors for tumor therapy
INVENTOR(S): Podhajcer, Osvaldo Luis; Ledda, Maria Fernanda; Adris, Soraya Karina; Bravo, Alicia Ines; Mordoh, Jose; Chernajovsky, Yuti
PATENT ASSIGNEE(S): Instituto de Investigaciones Bioquimicas Fundacion Campomar, Argent.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9829138 | A2 | 19980709 | WO 1997-GB3548 | 19971224 <-- |
| WO 9829138 | A3 | 19980917 | | |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| AU 9853332 | A1 | 19980731 | AU 1998-53332 | 19971224 <-- |
| EP 950097 | A2 | 19991020 | EP 1997-950334 | 19971224 <-- |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

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|---|---|---|---|
| PRIORITY APPLN. INFO.: | GB 1996-26989 | A | 19961227 |
| | US 1997-38068P | P | 19970212 |
| | WO 1997-GB3548 | W | 19971224 |

AB Compns. and methods are described that decrease or inhibit osteonectin activity in tumor cells, including cancer cells. The cells cease to be tumor-like, or become less tumor-like. Pharmaceutical compn. and therapies based thereon are also described.

L12 ANSWER 37 OF 48 CA COPYRIGHT 2003 ACS

| | |
|---|---|
| ACCESSION NUMBER: | 127:76008 CA |
| TITLE: | **Inhibition** of tumor growth by **antisense** oligonucleotides for **interleukin-8** (**IL-8**) and **IL-8** receptor |
| INVENTOR(S): | Pietrzkowski, Zbigniew; Cieslak, Dariusz; Olbina, Gordana |
| PATENT ASSIGNEE(S): | ICN Pharmaceuticals, USA |
| SOURCE: | PCT Int. Appl., 19 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 2 |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9719097 | A1 | 19970529 | WO 1996-US18406 | 19961116 <-- |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| CA 2236825 | AA | 19970529 | CA 1996-2236825 | 19961116 <-- |
| AU 9710531 | A1 | 19970611 | AU 1997-10531 | 19961116 <-- |
| AU 708096 | B2 | 19990729 | | |
| EP 879241 | A1 | 19981125 | EP 1996-941369 | 19961116 <-- |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

| | | | | |
|---|---|---|---|---|
| CN 1202900 | A | 19981223 | CN 1996-198451 | 19961116 <-- |
| JP 11507245 | T2 | 19990629 | JP 1997-519806 | 19961116 <-- |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 1995-561302 | A | 19951121 |
| | WO 1996-US18406 | W | 19961116 |

AB Oligonucleotides are provided which are effective in inhibiting the growth, metastasis and/or angiogenesis of tumors, including particularly melanoma and/or lung cancer. Methods are also provided for use of these oligonucleotides in the treatment of diseases.

L12 ANSWER 38 OF 48 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 126:26855 CA
TITLE: **Antisense** peptides for targeting to cytokines
INVENTOR(S): Miller, Andrew David; Raynes, John Graham
PATENT ASSIGNEE(S): Imperial College of Science, Technology and Medicine, UK; London School of Hygiene and Tropical Medicine; Miller, Andrew David; Raynes, John Graham
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9634887 | A2 | 19961107 | WO 1996-GB1082 | 19960507 <-- |
| WO 9634887 | A3 | 19970116 | | |

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN

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|---|---|---|---|---|
| AU 9656540 | A1 | 19961121 | AU 1996-56540 | 19960507 <-- |

PRIORITY APPLN. INFO.:
GB 1995-9263 19950505
GB 1996-7505 19960411
WO 1996-GB1082 19960507

AB An **antisense** peptide or polypeptide is claimed comprising an amino acid sequence which binds to a target peptide or polypeptide, thereby altering the biol. activity of the target peptide or polypeptide or the biol. activity of a target mol. which comprises the target peptide or polypeptide. The **antisense** peptide or polypeptide acts as an antagonist for or inhibitor of the target sequence or mol. In particular, the target mol. is a cytokine, e.g. IL-1.alpha. of IL-1.beta., TNF.alpha. or **IL-8** and the **antisense** peptides thus find use in treating or preventing conditions mediated by these cytokines, for instance inflammatory conditions or cancer. The **antisense** peptides were tested for biol. effect using an HuH7 hepatoma cell line system in which serum amyloid A (SAA) and heptoglobin were induced directly in response to IL-1. The peptides inhibited both IL-1.alpha. and IL-1.beta.-stimulated synthesis of SAA and heptoglobin in a dose dependent manner; SAA was inhibited more readily than heptoglobin.

L12 ANSWER 39 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:109686 CA
TITLE: Regulation of neural stem cell proliferation
INVENTOR(S): Weiss, Samuel; Reynolds, Brent A.
PATENT ASSIGNEE(S): Neurospheres Holdings Ltd., Can.
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9615226 | A1 | 19960523 | WO 1995-CA637 | 19951114 <-- |

W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,

SI, SK
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| US 5750376 | A | 19980512 | US 1995-483122 | 19950607 | <-- |
| US 5851832 | A | 19981222 | US 1995-486648 | 19950607 | <-- |
| AU 9538367 | A1 | 19960606 | AU 1995-38367 | 19951114 | <-- |
| AU 716811 | B2 | 20000309 | | | |
| EP 792350 | A1 | 19970903 | EP 1995-936393 | 19951114 | <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| CN 1170435 | A | 19980114 | CN 1995-196842 | 19951114 | <-- |
| JP 10509592 | T2 | 19980922 | JP 1995-515600 | 19951114 | <-- |
| FI 9701956 | A | 19970704 | FI 1997-1956 | 19970507 | <-- |
| NO 9702171 | A | 19970707 | NO 1997-2171 | 19970512 | <-- |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1994-338730 | A2 | 19941114 |
| US 1991-726812 | B2 | 19910708 |
| US 1992-961813 | B1 | 19921016 |
| US 1992-967622 | B1 | 19921028 |
| US 1993-10829 | B1 | 19930129 |
| US 1993-149508 | YY | 19931109 |
| US 1994-221655 | B1 | 19940401 |
| US 1994-270412 | B2 | 19940705 |
| US 1994-311099 | YY | 19940923 |
| US 1994-359345 | A | 19941220 |
| US 1994-359945 | B2 | 19941220 |
| US 1995-376062 | B2 | 19950120 |
| US 1995-385404 | B2 | 19950207 |
| WO 1995-CA637 | W | 19951114 |

AB The invention is directed to the regulation of multipotent neural stem cell proliferation in vitro and in vivo using compns. comprising various biol. factors. More particularly, the invention is related to a method and therapeutic compns. for regulating the no. of precursor cells that are produced by dividing neural stem cells, by exposing the stem cells to specific biol. factors or combinations thereof.

L12 ANSWER 40 OF 48 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 124:270541 CA
TITLE: Use of **antisense** nucleic acids/analogs **inhibiting** growth factor-mediated cell proliferation for treatment of proliferative and/or inflammatory skin disorders
INVENTOR(S): Werther, George Arthur; Wraight, Christopher John
PATENT ASSIGNEE(S): Royal Children's Hospital Research Foundation, Australia
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| WO 9601636 | A1 | 19960125 | WO 1995-AU410 | 19950706 | <-- |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT | | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2194366 | AA | 19960125 | CA 1995-2194366 | 19950706 | <-- |

| | | | | | |
|---|---|---|---|---|---|
| AU 9528753 | A1 | 19960209 | AU 1995-28753 | 19950706 | <-- |
| AU 692278 | B2 | 19980604 | | | |
| EP 776210 | A1 | 19970604 | EP 1995-924110 | 19950706 | <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| JP 10508286 | T2 | 19980818 | JP 1995-504013 | 19950706 | <-- |
| NZ 329202 | A | 20010831 | NZ 1995-329202 | 19950706 | <-- |
| US 5929040 | A | 19990727 | US 1996-666392 | 19960820 | <-- |
| US 6284741 | B1 | 20010904 | US 1998-199926 | 19981125 | <-- |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| AU 1994-6725 | A | 19940708 |
| WO 1995-AU410 | W | 19950706 |
| US 1996-666392 | A1 | 19960820 |

AB The present invention relates generally to a method for the prophylaxis and/or treatment of skin disorders, and in particular proliferative and/or inflammatory skin disorders, and to nucleic acids or nucleic acid analogs useful for same. The present invention is particularly directed to mols. capable of modulating growth factor interaction with its receptor on epidermal keratinocytes to inhibit, reduce or otherwise decrease stimulation of this layer of cells. The present invention contemplates, in a most preferred embodiment, a method for the prophylaxis and/or treatment of psoriasis. Phosphorothioate-linked oligonucleotide (18- and 24-mers) **antisense** to human insulin-like growth factor binding protein 3-encoding nucleic acid inhibited IGFBP-3 synthesis by HaCaT cells (human differentiated keratinocyte cell line).

L12 ANSWER 41 OF 48 CA COPYRIGHT 2003 ACS

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|---|---|
| ACCESSION NUMBER: | 124:115464 CA |
| TITLE: | Proteins binding the intracellular domains of TNF/NGF superfamily receptors and the formation of soluble oligomeric TNF/NGF superfamily receptors |
| INVENTOR(S): | Wallach, David; Boldin, Mark; Mett, Igor; Varfolomeev, Eugene |
| PATENT ASSIGNEE(S): | Yeda Research and Development Co., Ltd., Israel; Weinwurzel, Henry |
| SOURCE: | PCT Int. Appl., 95 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 1 |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| WO 9531544 | A1 | 19951123 | WO 1995-US5854 | 19950511 | <-- |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT | | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2189983 | AA | 19951123 | CA 1995-2189983 | 19950511 | <-- |
| AU 9525469 | A1 | 19951205 | AU 1995-25469 | 19950511 | <-- |
| AU 703919 | B2 | 19990401 | | | |
| ZA 9503842 | A | 19960117 | ZA 1995-3842 | 19950511 | <-- |
| EP 759984 | A1 | 19970305 | EP 1995-919787 | 19950511 | <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| CN 1152937 | A | 19970625 | CN 1995-194095 | 19950511 | <-- |
| JP 10500568 | T2 | 19980120 | JP 1995-529748 | 19950511 | <-- |
| FI 9604509 | A | 19970109 | FI 1996-4509 | 19961108 | <-- |
| NO 9604741 | A | 19970109 | NO 1996-4741 | 19961108 | <-- |
| AU 9897160 | A1 | 19990513 | AU 1998-97160 | 19981217 | <-- |
| AU 714907 | B2 | 20000113 | | | |

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|---|---|---|---|---|
| AU 9936902 | A1 | 19991104 | AU 1999-36902 | 19990630 <-- |
| AU 747029 | B2 | 20020509 | | |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| IL 1994-109632 | A | 19940511 |
| IL 1994-111125 | A | 19941002 |
| AU 1995-25469 | A3 | 19950511 |
| WO 1995-US5854 | W | 19950511 |

AB Novel proteins that bind the intracellular domains of the p55 and p75 TNF-Rs and the Fas-R, and that are capable of modulating the function of these receptors and the Fas antigen are identified and DNAs encoding them are described. Novel sol. oligomeric TNF-Rs, oligomeric Fas-Rs and mixed oligomeric receptors of TNF-Rs and Fas-Rs are also described. These oligomers can also inhibit TNF action. These novel proteins may be manufd. for therapeutic use, such as in the modulation of adverse effects from high levels of endogenous or administered tumor necrosis factors by inhibiting receptor function. Partial cDNAs for the receptor-binding proteins were cloned by screening in a yeast two-hybrid assay system with the intracellular domains of the p55 and p75 receptors as the ligand-binding domains and these were used to screen for full-length cDNAs. A no. of functional assays were used to identify the functionally important intracellular domains of the receptors.

L12 ANSWER 42 OF 48 SCISEARCH COPYRIGHT 2003 ISI (R)

ACCESSION NUMBER: 2001:491484 SCISEARCH

THE GENUINE ARTICLE: 441QG

TITLE: Helicobacter pylori-induced expression of **interleukin-8** and cyclooxygenase-2 in AGS gastric epithelial cells: Mediation by nuclear factor-kappa B

AUTHOR: Kim H; Lim J W; Kim K H (Reprint)

CORPORATE SOURCE: Yonsei Univ, Coll Med, Brain Korea Project Med Sci 21, Dept Pharmacol, Seoul 120752, South Korea (Reprint); Yonsei Univ, Coll Med, Brain Korea Project Med Sci 21, Inst Gastroenterol, Seoul 120752, South Korea

COUNTRY OF AUTHOR: South Korea

SOURCE: SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY, (**JUL 2001**) Vol. 36, No. 7, pp. 706-716. Publisher: TAYLOR & FRANCIS AS, CORT ADELERSGT 17, PO BOX 2562, SOLLI, 0202 OSLO, NORWAY. ISSN: 0036-5521.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 61

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Background: Helicobacter pylori infection might activate nuclear factor-kappaB (NF-kappaB), a transcriptional regulator of inducible expression of inflammatory genes, **interleukin-8** ( **IL-8**) and cyclooxygenase-2 (COX-2). We studied the role of NF-MB on expression of **IL-8** and COX-2 in H, pylori-stimulated AGS gastric epithelial cells by using **antisense** oligonucleotide: (AS ODN) for NF-kappaB subunit p50 and an antioxidant. glutathione (GSH) as well as a NF-kappaB inhibitor, pyrrolidine dithiocarbamate (PDTC). Methods: AGS cells were treated with p50 AS ODN. GSH or PDTC in the presence of H. pylori. mRNA expression and protein levels for **IL-8** and COX-2 were determined by Northern blot analysis and Western blot analysis. Levels of **IL-8** . 6-keto-prostaglandin F-1 alpha (6-keto-PGF(1 alpha)) and thromboxane B-2 (TXB2) were measured in the medium by enzyme-linked immunosorbent assay. NF-kappaB activation was examined by electrophoretic mobility shift assay. Results: H. pylori induced a time-dependent expression of mRNA and protein for **IL-8** and COX-2 via activation of NF-kappaB and increased the levels of **IL-8**. 6-keto-PGF(1 alpha), and TXB2. which were inhibited by GSH and PDTC. H, pylori-induced expression

of **IL-8** and COX-2 was blocked in AGS cells transfected with p50 AS ODN. Conclusion: NF-h B may play a novel role in expression of **IL-8** and COX-2 in H. pylori-induced gastric inflammation.

L12 ANSWER 43 OF 48 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 2001:305240 SCISEARCH
THE GENUINE ARTICLE: 418JU
TITLE: Nuclear factor-kappa B regulates cyclooxygenase-2 expression and cell proliferation in human gastric cancer cells
AUTHOR: Lim J W; Kim H (Reprint); Kim K H
CORPORATE SOURCE: Yonsei Univ, Coll Med, Dept Pharmacol, Seoul 120752, South Korea (Reprint); Yonsei Univ, Coll Med, Inst Gastroenterol, Brain Korea Project Med Sci 21, Seoul 120752, South Korea
COUNTRY OF AUTHOR: South Korea
SOURCE: LABORATORY INVESTIGATION, (**MAR 2001**) Vol. 81, No. 3, pp. 349-360.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA.
ISSN: 0023-6837.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 78

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Nuclear factor-kappaB (NF-kappaB) is a transcriptional regulator of inducible expression of genes including cyclooxygenase-2 (COX-2), regulating cell proliferation. NF-kappaB is kept silent in the cytoplasm via interaction with the inhibitory protein I kappaB alpha and transmigrated into the nucleus upon activation. However, constitutive NF-kappaB has been found in the nucleus of some cancer cells. We investigated the role of NF-kappaB in COX-2 expression and cell proliferation in human gastric cancer AGS cells. AGS cells were treated with **antisense** oligodeoxynucleotide (AS ODN) or sense oligodeoxynucleotide (S ODN) for the NF-kappaB subunit p50, or they were transfected with a mutated I kappaB alpha gene (MAD-3 mutant) or a control vector, pcDNA-3. AGS cells were treated with COX-2 inhibitors such as indomethacine and NS-398 or prostaglandin E-2. mRNA expression for COX-2, and protein levels for p50, I kappaB alpha, and COX-2 were determined by reverse transcription polymerase chain reaction and Western blot analysis. The NF-kappaB levels were examined by electrophoretic mobility shift assay. Thromboxane B-2 (TXB2) and 6-keto-prostaglandin F-1 alpha (6-keto-PGF(1 alpha)) levels were determined by enzyme-linked immunosorbent assay. Cell proliferation was assessed by viable cell counting, [H-3] thymidine incorporation, and colony formation. The nuclear level of p50 decreased in AGS cells treated with AS ODN. The I kappaB alpha mutant was observed in cells transfected with the mutated I kappaB alpha gene. NF-kappaB was inhibited in cells treated with AS ODN or transfected with the mutated I kappaB alpha gene, compared with the cells treated with S ODN or transfected with control vector. Cell proliferation, mRNA expression and protein level of COX-2, and production of TXB2 and 6-keto-PGF(1 alpha) were inhibited in cells treated with AS ODN or transfected with the mutated I kappaB alpha gene, which had lower NF-kappaB levels than cells treated with S ODN or transfected with control vector. COX-2 inhibitors suppressed cell proliferation and production of TXB2 and 6-keto-PGF(1 alpha), in a dose-dependant manner. Prostaglandin E, prevented the inhibition of proliferation in cells treated with AS ODN or transfected with the mutated I kappaB alpha gene. In conclusion, NF-kappaB mediates COX-2 expression, which may be related to cell proliferation, in human gastric cancer cells.

L12 ANSWER 44 OF 48 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 2001:144821 SCISEARCH
THE GENUINE ARTICLE: 398KQ
TITLE: An endoplasmic reticulum-specific stress-activated caspase (caspase-12) is implicated in the apoptosis of A549 epithelial cells by respiratory syncytial virus
AUTHOR: Bitko V; Barik S (Reprint)
CORPORATE SOURCE: Univ S Alabama, Coll Med, Dept Biochem & Mol Biol, 307 Univ BLvd, MSB 2370, Mobile, AL 36688 USA (Reprint); Univ S Alabama, Coll Med, Dept Biochem & Mol Biol, Mobile, AL 36688 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (**JAN 2001**) Vol. 80, No. 3, pp. 441-454.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012 USA.
ISSN: 0730-2312.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 58

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Respiratory syncytial virus (RSV) infection induced programmed cell death or apoptosis in the cultured lung epithelial cell line, A549. The apoptotic cells underwent multiple changes, including fragmentation and degradation of genomic DNA, consistent with the activation of the DNA fragmentation factor or caspase-activated DNase (DFF or CAD). The infection led to activation of FasL; however, a transdominant mutant of FAS-downstream death domain protein, FADD, did not inhibit apoptosis. Similarly, modest activation of cytoplasmic apoptotic caspases, caspase-3 and -8, were observed; however, only a specific inhibitor of caspases-3 inhibited apoptosis, while an inhibitor of caspase-8 had little effect. No activation of caspase-9 and -10, indicators of the mitochondrial apoptotic pathway, was observed. In contrast, RSV infection strongly activated caspase-12, an endoplasmic reticulum (ER) stress response caspase. Activation of the ER stress response was further evidenced by upregulation of ER chaperones BiP and calnexin. **Antisense**-mediated **inhibition** of caspase-12 **inhibited** apoptosis. Inhibitors of NF-kappa B had no effect on apoptosis. Thus, RSV-induced apoptosis appears to occur through an ER stress response that activates caspase-12, and is uncoupled from NF-kappa B activation. (C) 2001 Wiley-Liss, Inc.

L12 ANSWER 45 OF 48 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 2000:745485 SCISEARCH
THE GENUINE ARTICLE: 358MD
TITLE: Pseudomonas aeruginosa induction of apoptosis in respiratory epithelial cells - Analysis of the effects of cystic fibrosis transmembrane conductance regulator dysfunction and bacterial virulence factors
AUTHOR: Rajan S; Cacalano G; Bryan R; Ratner A J; Sontich C U; vanHeerckeren A; Davis P; Prince A (Reprint)
CORPORATE SOURCE: COLUMBIA UNIV COLL PHYS & SURG, DEPT PEDIAT INFECT DIS, 630 W 168TH ST, NEW YORK, NY 10032 (Reprint); COLUMBIA UNIV COLL PHYS & SURG, DEPT PEDIAT INFECT DIS, NEW YORK, NY 10032; CASE WESTERN RESERVE UNIV, DEPT PEDIAT, CLEVELAND, OH 44106
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY , (**SEP 2000**) Vol. 23, No. 3, pp. 304-312.
Publisher: AMER THORACIC SOC, 1740 BROADWAY, NEW YORK, NY 10019-4374.
ISSN: 1044-1549.
DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 35
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Airway epithelial cells can respond to infection by activating several signaling pathways. We examined the induction of apoptosis in response to Pseudomonas aeruginosa PAO1 in normal cells and several cystic fibrosis (CF) and corrected cell lines. Epithelial cells in monolayers with tight junctions, confirmed by apical ZO-1 staining demonstrated by confocal microscopy, were entirely resistant to PAO1-induced apoptosis. In contrast, cell lines such as 9HTEo(-) cells that do not form tight junctions were susceptible, with 50% of the population apoptotic after 6 h of exposure to PAO1, CF transmembrane conductance regulator (CFTR) dysfunction caused by different mechanisms (trafficking mutations, overexpression of the **regulatory** domain or **antisense** constructs) did not alter rates of apoptosis, nor were differences apparent in terminal deoxyribonucleotidyl transferase-mediated deoxyuridine triphosphate-biotin nick-end labeling detection of apoptotic airway cells from PAO1 infected cftr -/- or control mice. Bacterial expression of specific adhesins, complete lipopolysaccharide, and a functional type III secretion system were all necessary to evoke apoptosis even in susceptible epithelial cells. Unlike other mucosal surfaces, the airway epithelium is highly resistant to apoptosis, and this response is activated only when the appropriate epithelial conditions are present as well as fully virulent P. aeruginosa capable of coordinately expressing both adhesins and cytotoxins.

L12 ANSWER 46 OF 48 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 2000:645710 SCISEARCH
THE GENUINE ARTICLE: 345FV
TITLE: Entamoeba histolytica cysteine proteinases with interleukin-1 beta converting enzyme (ICE) activity cause intestinal inflammation and tissue damage in amoebiasis
AUTHOR: Zhang Z; Yan L; Wang L; Seydel K B; Li E; Ankri S; Mirelman D; Stanley S L (Reprint)
CORPORATE SOURCE: WASHINGTON UNIV, SCH MED, DEPT MED, ST LOUIS, MO 63110 (Reprint); WASHINGTON UNIV, SCH MED, DEPT MED, ST LOUIS, MO 63110; WEIZMANN INST SCI, DEPT BIOL CHEM, IL-76100 REHOVOT, ISRAEL; WASHINGTON UNIV, SCH MED, DEPT MOL MICROBIOL, ST LOUIS, MO 63110
COUNTRY OF AUTHOR: USA; ISRAEL
SOURCE: MOLECULAR MICROBIOLOGY, (**AUG 2000**) Vol. 37, No. 3, pp. 542-548.
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0950-382X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 23
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The protozoan parasite Entamoeba histolytica causes intestinal inflammation and ulceration. Amoebic trophozoites activate the transcription factor NF-kappa B in human intestinal epithelial cells, initiating an inflammatory response programme with resultant damage to the intestinal tissue. Amoebic cysteine proteinases have been proposed as important virulence factors for amoebiasis. To test the role of amoebic cysteine proteinases in the pathogenesis of amoebic colitis, human intestinal xenografts in SCID mice were infected with E. histolytica trophozoites expressing an **antisense** message to ehcp5. The cysteine proteinase-deficient amoeba failed to induce intestinal epithelial cell production of the inflammatory cytokines interleukin

(IL)-1B and **IL-8**, and caused significantly less gut inflammation and damage to the intestinal permeability barrier. The critical role of amoebic cysteine proteinases in human gut inflammation and tissue damage may be explained by our discovery that amoebic cysteine proteinases possess IL-1B converting enzyme (ICE) activity. This ICE activity could contribute to intestinal inflammation by activating human pIL-1B released by damaged intestinal cells. These results demonstrate for the first time that amoebic cysteine proteinases are a key virulence factor in amoebic colitis, and provide a novel mechanism for their activity.

L12 ANSWER 47 OF 48 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 2000:572436 SCISEARCH
THE GENUINE ARTICLE: 336ZZ
TITLE: **Antisense inhibition** of vascular endothelial growth factor in human and neck squamous cell carcinoma
AUTHOR: Nakashima T; Hudson J M; Clayman G L (Reprint)
CORPORATE SOURCE: UNIV TEXAS, MD ANDERSON CANC CTR, DEPT HEAD & NECK SURG, BOX 69, 1515 HOLCOMBE, HOUSTON, TX 77030 (Reprint); UNIV TEXAS, MD ANDERSON CANC CTR, DEPT HEAD & NECK SURG, HOUSTON, TX 77030
COUNTRY OF AUTHOR: USA
SOURCE: HEAD AND NECK-JOURNAL FOR THE SCIENCES AND SPECIALTIES OF THE HEAD AND NECK, (**AUG 2000**) Vol. 22, No. 5, pp. 483-488.
Publisher: JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 1043-3074.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 26

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Background. Vascular endothelial growth factor (VEGF) is a potent paracrine angiogenic factor involved in angiogenesis. We determined whether **antisense** VEGF transfection can suppress angiogenic activity of a human squamous cell carcinoma of the head and neck (SCCHN) cell line.

Methods. Human SCCHN cell lines were screened for VEGF secretion by ELISA. The highest VEGF secreting cell line was transfected with an **antisense** VEGF vector. Endothelial cell migration assays were performed using the conditioned medium from the transfected clones. Tumorigenicity assays of the transfectants in nude mice were also performed.

Results. **Antisense** VEGF expression exhibited a 20-fold inhibition of VEGF secretion. The addition of conditioned medium from the **antisense** clones resulted in 50% reduction of endothelial migration. There was no effect on in vivo tumorigenicity.

Conclusions. **Antisense** VEGF transfection effectively downregulated VEGF secretion from SCCHN cells that had high VEGF secretion. Targeting VEGF expression may be useful for suppressing angiogenesis in head and neck cancer. (C) 2000 John Wiley & Sons, Inc.

L12 ANSWER 48 OF 48 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 2000:107370 SCISEARCH
THE GENUINE ARTICLE: 279UX
TITLE: Laminar shear stress upregulates the complement-inhibitory protein clusterin - A novel potent defense mechanism against complement-induced endothelial cell activation
AUTHOR: Urbich C; Fritzenwanger M; Zeiher A M (Reprint); Dimmeler S

CORPORATE SOURCE: UNIV FRANKFURT, DEPT INTERNAL MED 4, DIV CARDIOL, THEODOR STERN KAI 7, D-60590 FRANKFURT, GERMANY (Reprint); UNIV FRANKFURT, DEPT INTERNAL MED 4, DIV CARDIOL, D-60590 FRANKFURT, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: CIRCULATION, (**1 FEB 2000**) Vol. 101, No. 4, pp. 352-355.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0009-7322.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 18

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Background-The complement system is implicated in the pathogenesis of atherosclerosis. Complement has been shown to activate endothelial cells (ECs) by inducing a proinflammatory response. Physiological levels of shear stress exert potent antiatherosclerotic effects. Therefore, we investigated whether shear stress antagonizes the effects of complement on ECs.

Methods and Results-Incubation of ECs with nonlytic concentrations of complement serum (CS: 0.2 U/mL for 6 hours) resulted in an upregulation of **interleukin-8** (**IL-8**) (165+/-12%) and monocyte chemoattractant protein-1 (MCP-I) mRNA expression (267+/-34%). Preexposure of ECs for 18 hours with laminar shear stress (15 dyne/cm(2)) abrogated CS-induced **IL-8** release to 106+/-10% ($P<0.001$) and reduced CS-induced MCP-1 expression (170+/-31%; $P<0.05$). To examine the mechanism of the protective effect of shear stress, expression of the complement-inhibitory protein clusterin was analyzed under shear exposure. Shear stress increased clusterin mRNA (225+/-76%, 6 hours) and protein expression (164+/-22%, 18 hours), Specific **inhibition** of clusterin by transfection with **antisense** oligonucleotides reversed the protective effect of shear stress on CS-induced MCP-1 and **IL-8** upregulation ($P<0.05$ versus sense-transfected cells). Moreover, clusterin overexpression inhibited CS-induced EC activation.

Conclusions-Shear stress abrogates the complement-induced proinflammatory response of ECs by upregulation of the complement-inhibitory protein clusterin, upregulation of clusterin may contribute to the potent antiatherosclerotic effects of shear stress by preventing endothelial activation through the complement cascade.